Amendments to the Specification

Please paragraphs [0022] to [0064] of the specification as filed with the following amended paragraphs:

[0022] Embodiment [0022]: The present invention comprises a compound for modulating p70S6K activity according to Formula I,

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

B, D, and E are each independently either =N- or = $C(R^2)$ -, provided at least one of B, D, and E is =N-;

at each occurance, each of R^1 , R^2 , and R^3 is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -OR⁵, -N(R⁵)OR⁵, -ON(R⁵)R⁵, -N(R⁵)N(R⁵)R⁵, -N(R⁵)R⁵, -S(O)₀₋₂R⁵, -SO₂N(R⁵)R⁵, -CO₂R⁵, -C(O)N(R⁵)R⁵, -N(R⁵)SO₂R⁵, -N(R⁵)C(O)R⁵, -N(R⁵)CO₂R⁵, -C(O)R⁵, -C(=NR⁷)N(R⁵)R⁵, -C(=NR⁷)N(R⁵)R⁵, optionally substituted lower alkyl, optionally substituted lower alkynyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl, and optionally substituted arylalkyl;

n is zero to five;

 R^4 is selected from -H, halogen, -CN, -NO₂, -N(R^5)OR⁵, -ON(R^5)R⁵, -N(R^5)N(R^5)R⁵, -OR⁵, -N(R^5)R⁵, -S(O)₀₋₂R⁵, -SO₂N(R^5)R⁵, -CO₂R⁵, -C(O)N(R^5)R⁵, -N(R^5)SO₂R⁵, -N(R^5)C(O)R⁵, -N(R^5)CO₂R⁵, -C(=NR⁷)N(R^5)R⁵, -C(=NR⁷)N(R^5)C(=NR⁷)N(R^5)R⁵, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted heterocyclylalkyl, and optionally substituted arylalkyl;

R² and R³, together with the atom or atoms to which they are attached, can combine to form a three- to seven-membered optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted cycloalkyl;

R² and R⁴, together with the atom or atoms to which they are attached, can combine to form a three- to seven-membered optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted cycloalkyl;

each R⁵ is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, optionally substituted lower heterocyclylalkyl, and a single bond to an atom of R¹;

two of R⁵, together with the atom or respective atoms to which they are attached, can combine to form an optionally substituted three- to seven-membered heterocyclic;

R⁵ and R⁶, together with the atom or atoms to which they are attached, can combine to form a five- to seven-membered optionally substituted heterocyclyl;

R⁵ and R⁷, together with the atom or atoms to which they are attached, can combine to form a five- to seven-membered optionally substituted heterocyclyl;

each of X and Y is independently selected from -C(=O)-, $-C(R^6)R^6$ -, -O-, $-N(R^5)$ -, $-C(=NR^7)$ -, and $-S(O)_{0-2}$ -; provided when X is -O- or $-N(R^5)$ -, then Y cannot be $-C(H)R^{6a}$ -, where R^{6a} is $-C(R^{20})(R^{21})R^{22}$ wherein at least one of R^{20} , R^{21} and R^{22} is selected from phenyl, napthyl, cyclohexyl, dihydronapthyl tetrahydronapthyl, and a five- to six-membered heteroaryl, each optionally substituted;

or X and Y can combine to form either $-C(R^6)=C(R^6)$ - or -C=C-;

Z is selected from O, S, and a double bond to an atom of R¹;

A is either $-N(R^5)$ - or a single bond;

each R^6 is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR⁵, -N(R⁵)R⁵, -S(O)₀₋₂R⁵, -SO₂N(R⁵)R⁵, -CO₂R⁵, -C(O)N(R⁵)R⁵, -N(R⁵)SO₂R⁵, -N(R⁵)C(O)R⁵, -N(R⁵)CO₂R⁵, -C(O)R⁵, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclylalkyl, optionally substituted arylalkyl, and a single bond to an atom of R² of D or E when said either D or E is =C(R²)-;

two of R^6 , together with the atom or atoms to which they are attached, can combine to form one of an optionally substituted three to seven-membered alicylic, an optionally substituted three to seven-membered heteroalicylic, and a double bond to an atom of R^2 of D or E when said either D or E is $=C(R^2)$ -;

each R^7 is independently selected from -H, -CN, -NO₂, -N(R^5) R^5 , -OR⁵, -S(O)₀₋₂ R^5 , -SO₂N(R^5) R^5 , -CO₂ R^5 , optionally substituted lower alkyl, optionally substituted lower alkynyl, and a single bond to a carbon of J; and

J is selected from an optionally substituted five- to ten-membered aryl and an optionally substituted five- to ten-membered heteroaryl;

provided the compound is not one of: 2-(2-amino-5-cyano-6-methylsulfanyl-pyrimidin-4ylsulfanyl)-N-(3-trifluoromethyl-phenyl)-acetamide, 2-{[2-amino-5-cyano-6-(methyl-2-{[2-amino-5-cyano-6thio)pyrimidin-4-yl]thio}-N-[3-(butyloxy)phenyl]acetamide, (methylthio)pyrimidin-4-yl]thio}-N-1,3-benzothiazol-2-ylacetamide, 2-{[2-amino-5-cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-(5-ethyl-1,3,4-thiadiazol-2-yl)acetamide, 2-{[2-amino-5cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-(4-methyl-1,3-thiazol-2-yl)acetamide, 2-amino-4-{[2-(3,5-dimethyl-1H-pyrazol-1-yl)-2-oxoethyl]thio}-6-(methylthio)pyrimidine-5-carbonitrile, 2-{[2-amino-5-cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-1,3-thiazol-2-ylacetamide, 2-(5cyano-2-methylsulfanyl-pyrimidin-4-ylsulfanyl)-N-phenyl-acetamide, 5-amino-2methylsulfanyl-thieno[2,3-d]pyrimidine-6-carboxylic acid phenylamide, 2-(6-amino-5-cyano-2methylsulfanyl-pyrimidin-4-ylsulfanyl)-N-phenyl-acetamide, 4,5-diamino-2-(2-methoxyethoxy)-thieno[2,3-d]pyrimidine-6-carboxylic acid phenylamide, 2-(5-cyano-6-phenyl-2phenylcarbamoylmethylsulfanyl-pyrimidin-4-ylsulfanyl)-N-phenyl-acetamide, and a 2-(6-amino-3,5-dicyano-pyridin-2-ylsulfanyl)-N-phenyl-acetamide derivative.

[0023] Embodiment [0023]: In one example, the compound is according to paragraph Embodiment [0022], wherein J is either a six-membered aryl or a five- to six-membered heteroaryl.

[0024] Embodiment [0024]: In another example, the compound is according to paragraph Embodiment [0023], wherein D is $=C(R^2)$ -.

[0025] Embodiment [0025]: In another example, the compound is according to paragraph Embodiment [0024], wherein R^4 is $-N(R^5)R^5$.

[0026] Embodiment [0026]: In another example, the compound is according to paragraph Embodiment [0025], of Formula II,

$$R^{5a} \underset{R}{\overset{B}{\overset{}}} = X \overset{H}{\overset{}} \underset{Q}{\overset{}} {\overset{Q}{\overset{}} {\overset{}} {\overset{Q}{\overset{}}} {\overset{Q}{\overset{}} {\overset{Q}{\overset{}}} {\overset{Q}$$

II

wherein, R^1 , R^2 , R^3 , R^5 , n, B, E, X, and Y are as defined above; and Q is either =N- or =C(H)-.

[0027] Embodiment [0027]: In another example, the compound is according to paragraph Embodiment [0026], wherein R^{2a} is selected from halogen, -CN, -C(=O)N(R^5) R^5 , -CF₃, -CO₂ R^5 , -C(R^5)=C(R^5) R^5 , -C=C- R^5 , and -NO₂;

[0028] Embodiment [0028]: In another example, the compound is according to paragraph Embodiment [0027], wherein at least one of R^{5a} and R^{5b} is -H.

[0029] Embodiment [0029]: In another example, the compound is according to paragraph Embodiment [0028], wherein R^3 is selected from $-OR^5$, $-NR^5R^5$, and $-S(O)_{0-2}R^5$.

[0030] Embodiment [0030]: In another example, the compound is according to paragraph Embodiment [0029], wherein at least one of B and E is =N-.

[0031] Embodiment [0031]: In another example, the compound is according to paragraph Embodiment [0030], wherein R¹ is selected from halogen, -OR⁵, -NR⁵R⁵, -S(O)₀₋₂R⁵, -NO₂, perhaloalkyl, optionally substituted lower alkyl, optionally substituted aryl, and optionally substituted arylalkyl.

[0032] Embodiment [0032]: In another example, the compound is according to paragraph Embodiment [0031], wherein R¹ is selected from halogen, -OR⁵, -NR⁵R⁵, -S(O)₀₋₁R⁵, -NO₂, perhaloalkyl, and optionally substituted lower alkyl.

[0033] Embodiment [0033]: In another example, the compound is according to paragraph Embodiment [0032], wherein A is $-N(R^5)$ -.

[0034] Embodiment [0034]: In another example, the compound is according to Embodiment paragraph [0033], of Formula III,

$$R^{5a} \underset{N}{\overset{R^3}{\bigvee}} X \underset{O}{\overset{N}{\bigvee}} \underset{Q}{\overset{R^{1a}}{\bigvee}} R^{1a}$$

Ш

wherein, R^3 , R^5 , X, Y, and Q are as defined above; R^{1a} is selected from halogen, lower perfluoroalkyl, $-NO_2$, $-OR^5$, and optionally substituted C_{1-4} alkyl; and R^{1b} is selected from halogen, $-OR^5$, $-N(R^5)R^5$, $-SR^5$, perfluoroalkyl, and optionally substituted lower alkyl.

[0035] Embodiment [0035]: In another example, the compound is according to Embodiment paragraph—[0034], wherein R^{1a} is selected from -NO₂, halogen, perfluoroalkyl, haloalkyl, optionally substituted C_{1-2} alkyl, and optionally substituted -O- C_{1-2} alkyl.

[0036] Embodiment [0036]: In another example, the compound is according to Embodiment paragraph—[0035], wherein R^3 is selected from optionally substituted -O-C₁₋₄alkyl, -O-C₁₋₄aperfluoroalkyl, optionally substituted -N(H)C₁₋₄alkyl, optionally substituted -N(C₁₋₄alkyl)C₁₋₄alkyl, optionally substituted -S(O)₀₋₂-C₁₋₄alkyl, and optionally substituted -S(O)₀₋₂-C₁₋₄aperfluoroalkyl.

[0037] Embodiment [0037]: In another example, the compound is according to Embodiment paragraph [0036], wherein Y is either -N(H)- or - $C(R^6)R^6$ -.

[0038] Embodiment [0038]: In another example, the compound is according to Embodiment paragraph [0037], wherein X is selected from -O-, -N(R⁵)- and -S-.

Embodiment [0039]: In another example, the compound is according to Embodiment paragraph-[0038], wherein Y is -C(R⁶)R⁶-; wherein each R⁶ is independently selected from -H, halogen, trihalomethyl, -NH₂, optionally substituted -O-C₁₋₄alkyl, optionally substituted -N(H)C₁₋₄alkyl, optionally substituted lower alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclylalkyl.

[0040] Embodiment [0040]: In another example, the compound is according to Embodiment paragraph—[0039], wherein Y is -C(H)R⁶-; wherein R⁶ is independently selected from -H, halogen, trihalomethyl, -NH₂, optionally substituted -O-C₁₋₄alkyl, optionally substituted -N(H)C₁₋₄alkyl, optionally substituted lower alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclylalkyl.

[0041] Embodiment [0041]: In another example, the compound is according to Embodiment paragraph [0040], wherein Q is =C(H)-.

[0042] <u>Embodiment [0042]:</u> In another example, the present invention comprises a compound for modulating p70S6K activity according to Formula **IV**,

or a pharmaceutically acceptable salt, hydrate, or prodrug thereof, wherein,

 R^1 is selected from halogen, $-OR^5$, $-N(R^5)R^5$, $-S(O)_{0-2}R^5$, $-NO_2$, $-C(O)R^5$, perhaloalkyl, optionally substituted lower alkyl, optionally substituted aryl, and optionally substituted arylalkyl.

n is zero to five;

 R^2 is selected from halogen, -CN, -C(=O)N(R^5) R^5 , -CF₃, -CO₂ R^5 , -C(R^5)=C(R^5) R^5 , -C=C- R^5 , and -NO₂;

 R^3 is selected from -H, halogen, trihalomethyl, -CN, -NO₂, -OR⁵, -N(R⁵)OR⁵, -ON(R⁵)R⁵, -N(R⁵)N(R⁵)R⁵, -N(R⁵)R⁵, -S(O)₀₋₂R⁵, -SO₂N(R⁵)R⁵, -CO₂R⁵, -C(O)N(R⁵)R⁵, -N(R⁵)SO₂R⁵, -N(R⁵)C(O)R⁵, -N(R⁵)CO₂R⁵, -C(O)R⁵, -C(=NR⁷)N(R⁵)R⁵, -C(=NR⁷)OR⁵, -C(=NR⁷)N(R⁵)R⁵, optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted arylalkyl;

 R^4 is selected from -CN, halogen, -NO₂, -N(R^5)OR⁵, -ON(R^5)R⁵, -N(R^5)N(R^5)R⁵, -OR⁵, -N(R^5)R⁵, -C(=NR⁷)N(R^5)R⁵, -C(=NR⁷)OR⁵, -C(=NR⁷)OR⁷, -C(=NR⁷)O

-N(R⁵)C(=NR⁷)N(R⁵)R⁵, optionally substituted lower alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclylalkyl;

each R⁵ is independently selected from -H, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, and optionally substituted lower heterocyclylalkyl;

two of R⁵, together with the atom or respective atoms to which they are attached, can combine to form an optionally substituted three- to seven-membered heterocyclic;

R⁵ and R⁶, together with the atom or atoms to which they are attached, can combine to form a five- to seven-membered optionally substituted heterocyclyl;

R⁵ and R⁷, together with the atom or atoms to which they are attached, can combine to form a five- to seven-membered optionally substituted heterocyclyl;

each of X and Y is independently selected from -C(=O)-, $-C(R^6)R^6$ -, -O-, $-N(R^5)$ -, $-C(=NR^7)$ -, and $-S(O)_{0-2}$ -; provided when X is -O- or $-N(R^5)$ -, then Y cannot be $-C(H)R^{6a}$ -, where R^{6a} is $-C(R^{20})(R^{21})R^{22}$ wherein at least one of R^{20} , R^{21} and R^{22} is selected from phenyl, napthyl, cyclohexyl, dihydronapthyl tetrahydronapthyl, and a five- to six-membered heteroaryl, each optionally substituted;

or X and Y can combine to form either $-C(R^6)=C(R^6)$ - or -C=C-;

each R^6 is independently selected from -H, halogen, trihalomethyl, -CN, -NO₂, -NH₂, -OR⁵, -N(R⁵)R⁵, -S(O)₀₋₂R⁵, -SO₂N(R⁵)R⁵, -CO₂R⁵, -C(O)N(R⁵)R⁵, -N(R⁵)SO₂R⁵, -N(R⁵)C(O)R⁵, -N(R⁵)CO₂R⁵, -C(O)R⁵, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted heterocyclyl, optionally substituted arylalkyl, and a single bond to an atom of R¹;

two of R⁶, together with the atom or atoms to which they are attached, can combine to form either an optionally substituted three to seven-membered alicylic or an optionally substituted three to seven-membered heteroalicylic;

each R^7 is independently selected from -H, -CN, -NO₂, -N(R^5) R^5 , -OR⁵, -S(O)₀₋₂ R^5 , -SO₂N(R^5) R^5 , -CO₂ R^5 , optionally substituted lower alkyl, optionally substituted lower alkenyl, optionally substituted lower alkynyl, and a single bond to a carbon of J; and

J is selected from an optionally substituted five- to ten-membered aryl and an optionally substituted five- to ten-membered heteroaryl;

provided the compound is not one of: 2-(2-amino-5-cyano-6-methylsulfanyl-pyrimidin-4ylsulfanyl)-N-(3-trifluoromethyl-phenyl)-acetamide, 2-{[2-amino-5-cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-[3-(butyloxy)phenyl]acetamide, 2-{[2-amino-5-cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-1,3-benzothiazol-2-ylacetamide, 2-{[2-amino-5-cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-(5-ethyl-1,3,4-thiadiazol-2-yl)acetamide, 2-{[2-amino-5cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-(4-methyl-1,3-thiazol-2-yl)acetamide, 2-amino-4-{[2-(3,5-dimethyl-1H-pyrazol-1-yl)-2-oxoethyl]thio}-6-(methylthio)pyrimidine-5-carbonitrile, 2-{[2-amino-5-cyano-6-(methylthio)pyrimidin-4-yl]thio}-N-1,3-thiazol-2-ylacetamide, 2-(5cyano-2-methylsulfanyl-pyrimidin-4-ylsulfanyl)-N-phenyl-acetamide, 5-amino-2methylsulfanyl-thieno[2,3-d]pyrimidine-6-carboxylic acid phenylamide, 2-(6-amino-5-cyano-2methylsulfanyl-pyrimidin-4-ylsulfanyl)-N-phenyl-acetamide, 4,5-diamino-2-(2-methoxyethoxy)-thieno[2,3-d]pyrimidine-6-carboxylic acid phenylamide, 2-(5-cyano-6-phenyl-2phenylcarbamovlmethylsulfanyl-pyrimidin-4-ylsulfanyl)-N-phenyl-acetamide, and a 2-(6-amino-3,5-dicyano-pyridin-2-ylsulfanyl)-N-phenyl-acetamide derivative.

- [0043] Embodiment [0043]: In another example, the compound is according to Embodiment paragraph [0042], wherein R⁴ is -NR^{5a}R^{5b}; wherein at least one of R^{5a} and R^{5b} is -H.
- [0044] Embodiment [0044]: In another example, the compound is according to Embodiment paragraph [0043], wherein X is selected from -O-, -N(R⁵)-, and -S(O)₀₋₂-.
- [0045] Embodiment [0045]: In another example, the compound is according to Embodiment paragraph [0044], wherein Y is either $-C(R^6)R^6$ or $-N(R^5)$ -.
- [0046] Embodiment [0046]: In another example, the compound is according to Embodiment paragraph [0045], wherein J is either phenyl or pyridyl.
- [0047] Embodiment [0047]: In another example, the compound is according to Embodiment paragraph [0046], wherein R⁴ is -NH₂.
- [0048] Embodiment [0048]: In another example, the compound is according to Embodiment paragraph-[0047], wherein at least one of R^1 is selected from halo, -NO₂, -OR⁵, perfluoroalkyl, haloalkyl, and optionally substituted C_{1-4} alkyl.

[0049] Embodiment [0049]: In another example, the compound is according to Embodiment paragraph [0048], of Formula V,

$$H_2N$$
 N
 X
 Y
 N
 Q
 R^{1a}
 R^{1a}

wherein R^1 , R^3 , X, and Y are as defined above; and Q is either =N- or =C(H)-.

[0050] Embodiment [0050]: In another example, the compound is according to Embodiment paragraph—[0049], wherein R^{1a} is selected from halo, lower perfluoroalkyl, -NO₂, optionally substituted -O-C₁₋₄alkyl, and optionally substituted C₁₋₄alkyl.

[0051] Embodiment [0051]: In another example, the compound is according to Embodiment paragraph—[0050], wherein R^3 is selected from optionally substituted -O-C₁₋₄alkyl, -O-C₁₋₄alkyl, optionally substituted -N(H)C₁₋₄alkyl, optionally substituted -N(C₁₋₄alkyl)C₁₋₄alkyl, optionally substituted -S(O)₀₋₂-C₁₋₄alkyl, and optionally substituted -S(O)₀₋₂-C₁₋₄alkyl.

Embodiment [0052]: In another example, the compound is according to Embodiment paragraph-[0051], wherein Y is -C(R⁶)R⁶-; wherein each R⁶ is independently selected from -H, halogen, trihalomethyl, -NH₂, optionally substituted -O-C₁₋₄alkyl, optionally substituted -N(H)C₁₋₄alkyl, optionally substituted lower alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclylalkyl.

Embodiment [0053]: In another example, the compound is according to Embodiment paragraph—[0052], wherein Y is -C(H)R⁶-; wherein R⁶ is independently selected from -H, halogen, trihalomethyl, -NH₂, optionally substituted -O-C₁₋₄alkyl, optionally substituted -N(H)C₁₋₄alkyl, optionally substituted lower alkyl, optionally substituted heterocyclyl, and optionally substituted heterocyclylalkyl.

[0054] Embodiment [0054]: In another example, the compound is according to Embodiment paragraph [0053], wherein Q is =C(H)-.

[0055] Embodiment [0055]: In another example, the compound is according to Embodiment paragraph [0022], selected from

Table 1

Entry	Name	Structure
1	2-[(3-cyano-4,6-dimethyl-5- nitropyridin-2-yl)oxy]-N-[3- (trifluoromethyl)phenyl]acetamide	O_2N CN N CF_3
2	N-2-(2-amino-6-chloropyrimidin-4- yl)-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N
3	[2-amino-6-(methylthio)pyrimidin-4- yl]methyl [3- (trifluoromethyl)phenyl]carbamate	H_2N N O O CF_3
4	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [5-(trifluoromethyl)pyridin-2- yl]acetamide	H_2N N S CN H N S CF_3
5	N-2-[2-amino-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N
6	2-{[2-amino-6-(methylthio)pyrimidin- 4-yl]oxy}-N-[3- (trifluoromethyl)phenyl]acetamide	S N

Table 1

Entry	Name	Structure
7	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [3-(methyloxy)phenyl]acetamide	H_2N N N N N N N N N N
8	N-2-(2-amino-6-morpholin-4- ylpyrimidin-4-yl)-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N
9	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- (4-chlorophenyl)acetamide	H ₂ N CI
10	2-{[2-amino-6-(1H-1,2,3-benzotriazol-1-yloxy)pyrimidin-4-yl]thio}-N-[3-(trifluoromethyl)phenyl]acetamide	NH ₂ N N N CF ₃ CF ₃
11	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- (3-chlorophenyl)acetamide	H_2N N N N N N N N N N
12	N-2-(2-amino-6-chloro-5- formylpyrimidin-4-yl)-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N

Table 1

Entry	Name	Structure
13	N-2-[2-amino-5-formyl-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	H ₂ N N N CF ₃
14	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]oxy}-N- [3-(trifluoromethyl)phenyl]acetamide	H ₂ N H ₂ N F F
15	2-[(2-amino-6-chloropyrimidin-4-yl)thio]-N-[3-(trifluoromethyl)phenyl]acetamide	CI N
16	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- methyl-N-[3- (trifluoromethyl)phenyl]acetamide	H ₂ N N S N CF ₃
17	N-2-[4-amino-6-(methylthio)-1,3,5- triazin-2-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N
18	N-2-[4-(dimethylamino)-6- (methylthio)-1,3,5-triazin-2-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	S N N N N CF3

Table 1

Entry	Name	Structure
19	N-2-[4-(methylamino)-6- (methylthio)-1,3,5-triazin-2-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	S N N N N CF3
20	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N
21	'2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [3-(trifluoromethyl)phenyl]acetamide	NH ₂ S S S S S S S S S S S S S S S S S S S
22	'2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [3-(butyloxy)phenyl]acetamide	NH ₂ S NH ₂
23	'2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- 1,3-benzothiazol-2-ylacetamide	H ₂ N N S O S HN N
24	'2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- (5-ethyl-1,3,4-thiadiazol-2- yl)acetamide	S NH NH ₂
25	'2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- (4-methyl-1,3-thiazol-2-yl)acetamide	NH ₂

Table 1

Entry	Name	Structure
26	'2-amino-4-{[2-(3,5-dimethyl-1H-pyrazol-1-yl)-2-oxoethyl]thio}-6-(methylthio)pyrimidine-5-carbonitrile	S N N N N N N N N N N N N N N N N N N N
27	'2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- 1,3-thiazol-2-ylacetamide	NH ₂ N N N N N N N N N N N N N N N N N N N
28	ethyl 5-[({[2-amino-5-cyano-6- (methylthio)pyrimidin-4- yl]thio}acetyl)amino]-4-cyano-3- methylthiophene-2-carboxylate	H ₂ N N S NC NC
29	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- pyridin-2-ylacetamide	H_2N N S CN N N N N N N N N N
30	2-amino-4-({2-[2,5-bis(methyloxy)phenyl]-2-oxoethyl}thio)-6-(methylthio)pyrimidine-5-carbonitrile	H_2N N S CN O O O
31	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [4-fluoro-3- (trifluoromethyl)phenyl]acetamide	H_2N N S CN H CF_3 F

Table 1

Entry	Name	Structure
32	2-[(2,6-diaminopyrimidin-4-yl)thio]- N-[4-fluoro-3- (trifluoromethyl)phenyl]acetamide	H_2N N S CF_3 F
33	2-[(2,6-diaminopyrimidin-4-yl)thio]- N-[3- (trifluoromethyl)phenyl]acetamide	H_2N N S CF_3
34	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [4-chloro-3- (trifluoromethyl)phenyl]acetamide	H_2N N S CN H_2N CF_3 CI
35	2-amino-4-(methylthio)-6-({2-oxo-1-[3-(trifluoromethyl)phenyl]pyrrolidin-3-yl}thio)pyrimidine-5-carbonitrile	H_2N N S CN N S CF_3
36	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [6-(trifluoromethyl)pyridin-2- yl]acetamide	H_2N N S CN H N CF_3
37	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [4-(trifluoromethyl)pyridin-2- yl]acetamide	H_2N N S CN H S CF_3

Table 1

Entry	Name	Structure
38	{6-(methylthio)-2- [(phenylmethyl)amino]pyrimidin-4- yl}methyl [3- (trifluoromethyl)phenyl]carbamate	S CF ₃
39	[6-(methylamino)-2- (methylthio)pyrimidin-4-yl]methyl [3- (trifluoromethyl)phenyl]carbamate	S N O H CF3
40	{2-(methylthio)-6- [(phenylmethyl)amino]pyrimidin-4- yl}methyl [3- (trifluoromethyl)phenyl]carbamate	S N O H CF3
41	2-{[2-(acetylamino)-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [3-(trifluoromethyl)phenyl]acetamide	N H S F F
42	(2S)-2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]oxy}-N- [3- (trifluoromethyl)phenyl]propanamide	-s N
43	2-[(2-amino-6-chloro-5- formylpyrimidin-4-yl)thio]-N-[3- (trifluoromethyl)phenyl]acetamide	NH ₂ N N F F

Table 1

Entry	Name	Structure
44	N-2-[2-amino-5-(hydroxymethyl)-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	NH ₂ N N N N N N N N N N N N N N N N N N N
45	2-{[2-amino-5-formyl-6- (methylamino)pyrimidin-4-yl]thio}- N-[3- (trifluoromethyl)phenyl]acetamide	NH ₂ S S F F
46	2-{[2-amino-5-formyl-6- (methylthio)pyrimidin-4-yl]oxy}-N- [3-(trifluoromethyl)phenyl]acetamide	NH ₂ N N N N N N N N N N N N N N N N N N N
47	2-{[4-amino-6-(methylthio)-1,3,5- triazin-2-yl]oxy}-N-[3- (trifluoromethyl)phenyl]acetamide	H ₂ N N O H F F
48	2-{[2-amino-6-(methylthio)pyrimidin-4-yl]thio}-N-[3-(trifluoromethyl)phenyl]acetamide	S N N N N N N N N N N N N N N N N N N N
49	2-amino-4-(methylthio)-6-{[2-oxo-2-(3-oxo-3,4-dihydro-2H-1,4-benzoxazin-6-yl)ethyl]thio}pyrimidine-5-carbonitrile	$\begin{array}{c} & & & \\$
50	2-[(2-amino-6-chloro-5- formylpyrimidin-4-yl)oxy]-N-[3- (trifluoromethyl)phenyl]acetamide	NH ₂ N N N N N N N N N N N N N N N N N N N

Table 1

Entry	Name	Structure
51	2-{[2-amino-5-formyl-6-(phenylthio)pyrimidin-4-yl]thio}-N-[3-(trifluoromethyl)phenyl]acetamide	$S \downarrow N \downarrow N \downarrow N \downarrow F \downarrow F \downarrow F$
52	2-{[2-amino-5-(hydroxymethyl)-6-(phenylthio)pyrimidin-4-yl]thio}-N-[3-(trifluoromethyl)phenyl]acetamide	S N N N F F
53	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [2-methyl-3- (trifluoromethyl)phenyl]acetamide	H_2N N N N N N N N N N
54	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [2-(methyloxy)-5- (trifluoromethyl)phenyl]acetamide	H_2N N S N
55	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [2-chloro-5- (trifluoromethyl)phenyl]acetamide	H ₂ N N S N H CI
56	2-{[2-amino-5-(hydroxymethyl)-6-(methylthio)pyrimidin-4-yl]oxy}-N-[3-(trifluoromethyl)phenyl]acetamide	NH ₂ N N N F F

Table 1

Entry	Name	Structure
57	N-2-(6-amino-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-N-[3-(trifluoromethyl)phenyl]glycinamide	NH ₂ N N N N N N N N N N N N N N N N N N N
58	N-2-[2-amino-5-[(E)- hydrazonomethyl]-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	NH ₂ N N N N N N N N N N N N N N N N N N N
59	N-2-[2-amino-5-[(E)- (hydroxyimino)methyl]-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	NH ₂
60	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L- alaninamide	S CN H O F F
61	2-{[2-amino-5-cyano-6- (methylamino)pyrimidin-4-yl]thio}- N-[3- (trifluoromethyl)phenyl]acetamide	NH N N N S N N F F
62	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [2-amino-5- (trifluoromethyl)phenyl]acetamide	H ₂ N N S N H NH ₂

Table 1

Entry	Name	Structure
63	2-amino-4-(methylthio)-6-({[6- (trifluoromethyl)-1H-benzimidazol-2- yl]methyl}thio)pyrimidine-5- carbonitrile	H ₂ N S N F F
64	2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]hydrazinecar boxamide	$ \begin{array}{c} $
65	N-2-[5-cyano-2-(methylamino)-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	N N N N N N N N N N N N N N N N N N N
66	2-{[2-amino-5-cyano-6- (dimethylamino)pyrimidin-4-yl]thio}- N-[3- (trifluoromethyl)phenyl]acetamide	H ₂ N S
67	(S)-1-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]prolinamide	N H N H
68	(2R)-2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]oxy}-N- [3- (trifluoromethyl)phenyl]propanamide	-S N F F F F F F F F F F F F F F F F F F

Table 1

Entry	Name	Structure
69	1-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]oxy}-N- [3- (trifluoromethyl)phenyl]cyclopropane carboxamide	N N N N N N H ₂ N
70	(2S)-2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]oxy}-3- methyl-N-[3- (trifluoromethyl)phenyl]butanamide	H_2N N N N N N N N N N
71	N-2-[5-cyano-2-(dimethylamino)-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z
72	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-2- methyl-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N
73	1-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]amino}- N-[3- (trifluoromethyl)phenyl]cyclopropane carboxamide	$-S$ H_2N H_2N H_3 H_4 H_5
74	N-2-[2-amino-5-cyano-6- (methylsulfinyl)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L- alaninamide	H ₂ N N H F F

Table 1

Entry	Name	Structure
75	N-2-[2-amino-5-cyano-6- (methylsulfonyl)pyrimidin-4-yl]-N- [3-(trifluoromethyl)phenyl]-L- alaninamide	O=S N N N N N N N N N N N N N
76	N-2-(5-cyano-2-morpholin-4- ylpyrimidin-4-yl)-N-[3- (trifluoromethyl)phenyl]glycinamide	N H S F F
77	2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]thio}-N- [3,5- bis(trifluoromethyl)phenyl]acetamide	H_2N N S N CF_3 CF_3 CF_3
78	N-2-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L- alaninamide	H_2N N N N N N N N N N
79	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[2- (methyloxy)-5- (trifluoromethyl)phenyl]-L- alaninamide	H_2N N N N N N N N N N
80	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[2- chloro-5-(trifluoromethyl)phenyl]-L- alaninamide	H_2N N N N N N N N N N

Table 1

Entry	Name	Structure
81	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-2- methyl-N-[3- (trifluoromethyl)phenyl]alaninamide	H_2N N N N N N N N N N
82	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-{3-[(4- methylpiperazin-1- yl)carbonyl]phenyl}-L-alaninamide	$\begin{array}{c} & & & \\$
83	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-D- alaninamide	H_2N N N N N N N N N N
84	2-[(2-amino-5-cyano-6-morpholin-4-ylpyrimidin-4-yl)thio]-N-[3-(trifluoromethyl)phenyl]acetamide	NH ₂ N N S N F F
85	(R)-1-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]prolinamide	H ₂ N N O F F
86	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L- ornithinamide	S CN H ₂ CF ₃

Table 1

Entry	Name	Structure
87	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-2-[2- (dimethylamino)ethyl]-N-[3- (trifluoromethyl)phenyl]glycinamide	S CN H ₂ N CF ₃
88	N-2-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L- alaninamide	H_2N N N N N N N N N N
89	N-2-(2,6-diamino-5-cyanopyrimidin-4-yl)-N-[3-(trifluoromethyl)phenyl]-L-alaninamide	H_2N N N N N N N N N N
90	N-2-(2-amino-5-cyanopyrimidin-4-yl)-N-[3-(trifluoromethyl)phenyl]-L-alaninamide	H_2N N N N N N N N N N
91	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-2- methyl-N-[3- (trifluoromethyl)phenyl]-L- alaninamide	H_2N N N N N N N N N N
92	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-(3-{[2- (diethylamino)ethyl]oxy}phenyl)-L- alaninamide	S CN H

Table 1

Entry	Name	Structure
93	2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-1,2- dimethyl-N-[3- (trifluoromethyl)phenyl]hydrazinecar boxamide	H_2N N N N N N N N N N
94	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- amino-5-(trifluoromethyl)phenyl]-L- alaninamide	H_2N N N N N N N N N N
95	ethyl [1-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-2-({[3- (trifluoromethyl)phenyl]amino}carbo nyl)hydrazino]acetate	$\begin{array}{c c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$
96	2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-2- methyl-N-[3- (trifluoromethyl)phenyl]hydrazinecar boxamide	H_2N N N N N N N N N N
97	3,5-diamino-4,6-dimethyl-N-[3- (trifluoromethyl)phenyl]furo[2,3- b]pyridine-2-carboxamide	H_2N N N N N N N N N N
98	3-amino-4,6-dimethyl-5-nitro-N-[3- (trifluoromethyl)phenyl]furo[2,3- b]pyridine-2-carboxamide	O_2N NH_2 H CF_3

Table 1

Entry	Name	Structure
99	N-2-(2-amino-5-cyano-6- hydroxypyrimidin-4-yl)-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	H_2N N N N N N N N N N
100	N-2-[5-cyano-2-(methylthio)pyrimidin-4- yl]-N-[3- (trifluoromethyl)phenyl]glycinamide	S N N N CF3
101	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-2- (tetrahydro-2H-pyran-4-ylmethyl)-N-[3- (trifluoromethyl)phenyl]glycinamide	H_2N N N N N N N N N N
102	N-2-(2-amino-5-cyano-6-{[2- (dimethylamino)ethyl]oxy}pyrimidin-4-yl)- N-[3-(trifluoromethyl)phenyl]-L- alaninamide	H_2N N N N N N N N N N
103	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-6-{[(1,1- dimethylethyl)oxy]carbonyl}-N-[3- (trifluoromethyl)phenyl]-L-lysinamide	S CN CF3 CF3 CF3 CF3 NH2 NH CN NH CN
104	2-amino-4-(methylthio)-6-(methyl{(1S)-1- [6-(trifluoromethyl)-1H-benzimidazol-2- yl]ethyl}amino)pyrimidine-5-carbonitrile	N N N N N N N N N N

Table 1

Entry	Name	Structure
105	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-2-[2- (tetrahydro-2H-pyran-4-yl)ethyl]-N-[3- (trifluoromethyl)phenyl]glycinamide	S CN CF3
106	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3-{[2- (diethylamino)ethyl]amino}-5- (trifluoromethyl)phenyl]-L-alaninamide	S NH ₂ N NH N NH N NH CF ₃
107	2-amino-4-(methylthio)-6-({(1S)-1-[6- (trifluoromethyl)-1H-benzimidazol-2- yl]ethyl}amino)pyrimidine-5-carbonitrile	-s N
108	2-{2-amino-5-cyano-6-[1-(3- trifluoromethyl-phenylcarbamoyl)-1S- ethylamino]-pyrimidin-4-ylamino}-N-(3- trifluoromethyl-phenyl)-2S-propionamide	H_2N N H_2N N H_2N N H_3 N H_4 N H_5 N
109	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-2-methyl-N- (3-methylphenyl)glycinamide	S NH2 N N N N N N N N N N N N N N N N N N N
110	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-2-methyl-N- [3-(1-methylethyl)phenyl]glycinamide	NH ₂ N N N N N N N N N N N N N N N N N N N

Table 1

Entry	Name	Structure
111	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-5- [imino(nitroamino)methyl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	NH ₂ N NO ₂ CF ₃
112	methyl 3-({N-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-L- alanyl}amino)-5-(trifluoromethyl)benzoate	S NH ₂ N N N N N N N N N N N N N N N N N N N
113	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-(3- nitrophenyl)-L-alaninamide	S NH ₂ N N N N N N NO ₂ NO ₂
114	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-lysinamide	S NH2 NH2 CF3
115	N-2-[2-amino-5-cyano-6- (propyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	NH ₂ NH ₂ NH ₂ NH ₂ CF ₃
116	N-2-[5-cyano-2-{[2- (methyloxy)ethyl]amino}-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	S CN H O CF3

Table 1

Entry	Name	Structure
117	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-argininamide	NH ₂ NH ₂ NH CF ₃
118	N-2-[2-amino-5-cyano-6- (methylsulfinyl)pyrimidin-4-yl]-N-2-methyl- N-[3-(trifluoromethyl)phenyl]-L- alaninamide	NH ₂ N N N N N N N N N N N N N N N N N N N
119	N-2-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-N-2-methyl-N- [3-(trifluoromethyl)phenyl]-L-alaninamide	NH ₂ N N N CF ₃ CF ₃
120	N-2-[2-amino-5-cyano-6- (propyloxy)pyrimidin-4-yl]-N-2-methyl-N- [3-(trifluoromethyl)phenyl]-L-alaninamide	NH ₂ NH ₂ NH ₂ CF ₃
121	N-2-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-2-methyl-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	NH ₂ N N CF ₃ CF ₃
122	N-2-{2-amino-5-cyano-6-[(1- methylethyl)oxy]pyrimidin-4-yl}-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	NH ₂ N N N N N N N N N N N N N N N N N N N

Table 1

Entry	Name	Structure
123	N-5-acetyl-N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	NH ₂ NH ₂ NH ₂ NH ₂ CF ₃
124	N-2-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-(3- aminophenyl)-L-alaninamide	S NH ₂
125	3-({N-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-L- alanyl}amino)-N-[2-(dimethylamino)ethyl]- 5-(trifluoromethyl)benzamide	NH ₂ NH ₂ NH NH NH NH CF ₃
126	2-(methyloxy)ethyl ((4S)-4-{[2-amino-5- cyano-6-(methylthio)pyrimidin-4- yl]amino}-5-oxo-5-{[3- (trifluoromethyl)phenyl]amino}pentyl)carb amate	NH ₂ N N N CF ₃ CCF ₃
127	2-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]hydrazinecarboxa mide	NH ₂ N H H H CF ₃ CF ₃
128	1,1-dimethylethyl ((4S)-4-{[2-amino-5-cyano-6-(ethyloxy)pyrimidin-4-yl]amino}-5-oxo-5-{[3-(trifluoromethyl)phenyl]amino}pentyl)carbamate	NH_2

Table 1

Entry	Name	Structure
129	N-2-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	NH ₂ NH ₂ NH ₂ CF ₃
130	3-({N-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-methyl-L- alanyl}amino)-N-[2- (dimethylamino)ethyl]-5- (trifluoromethyl)benzamide	H ₂ N N CH ₃ H CF ₃ H ₃ C N CH ₃
131	3-({N-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-methyl-L- alanyl}amino)-N-[3-(4-methylpiperazin-1- yl)propyl]-5-(trifluoromethyl)benzamide	S.CH ₃ Chiral N CH ₃ H CH ₃ H CF ₃ CH ₃ O CH
132	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N~2~-methyl- N-{3-[(trifluoromethyl)oxy]phenyl}-L- alaninamide	Chiral N CH ₃ H O F F F

Table 1

Entry	Name	Structure
133	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-(3- bromophenyl)-N~2~-methyl-L- alaninamide	H ₃ C·s Chiral H ₂ N N N N N N Br CH ₃ O
134	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-{2-{[2- (dimethylamino)ethyl]oxy}-5- [(trifluoromethyl)oxy]phenyl}-N~2~- methyl-L-alaninamide	S.CH ₃ N CH ₃ H CH ₃ O F F H ₃ C.N.CH ₃
135	3-({N-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-methyl-L- alanyl}amino)-N-(2-morpholin-4-ylethyl)- 5-(trifluoromethyl)benzamide	Chiral Chiral Page 19
136	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N~2~-methyl-N- [3-(trifluoromethyl)phenyl]-L-lysinamide	CH ₃ NH ₂ Chiral H ₂ N N N N F F

Table 1

Entry	Name	Structure
137	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3-{[2- (dimethylamino)ethyl]oxy}-5- (trifluoromethyl)phenyl]-L-alaninamide	S.CH ₃ N F F F O N CH ₃ CH ₃ CH ₃ CH ₃ CH ₃
138	(2S)-2-{[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]amino}-3-oxo- 3-{[3-(trifluoromethyl)phenyl]amino}propyl acetate	H ₃ C·S O CH ₃ Chiral H ₂ N N N CF ₃
139	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N~1~-[3- (trifluoromethyl)phenyl]-L-glutamamide	H ₃ C.S.H ₂ NO Chiral H ₂ NNNNN CF ₃
140	2-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]hydrazinecarboxa mide	H ₃ C. O H H H F F F F F
141	3-({N-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-L- alanyl}amino)-N-hydroxy-5- (trifluoromethyl)benzamide	S.CH ₃ N CH ₃ H CF ₃ HNO OOH

Table 1

Entry	Name	Structure
142	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-3- (dimethylamino)-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	H ₃ C. S Chiral Chiral Chiral Chiral Chiral
143	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-5-morpholin-4- yl-N-[3-(trifluoromethyl)phenyl]-L- norvalinamide	H ₃ C.S.N.H.F.F.F.F.F.F.F.F.F.F.F.F.F.F.F.F.F.F
144	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N~5~-[2- (methyloxy)ethyl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	S.CH3 Chiral NH H ₂ N N CF ₃
145	3-({N-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-L- alanyl}amino)-5-(trifluoromethyl)benzoic acid	S.CH ₃ N CH ₃ H CF ₃ HOOO
146	methyl N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alpha- glutaminate	H ₃ C S H ₃ C O O Chiral H ₂ N N N CF ₃

Table 1

Entry	Name	Structure
147	N~5~-(aminocarbonyl)-N~2~-[2-amino-5-cyano-6-(methylthio)pyrimidin-4-yl]-N-[3-(trifluoromethyl)phenyl]-L-ornithinamide	ONH ₂ Chiral NH NH NH NH NH NH NH NH NH N
148	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	CH ₃ NH ₂ NH ₂ H ₂ N N N F F
149	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alpha-glutamine	H ₃ C·s HO O Chiral H ₂ N N N CF ₃
150	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-serinamide	CH ₃ CN OH H ₂ N N N CF ₃
151	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-O- (phenylmethyl)-N-[3- (trifluoromethyl)phenyl]-L-serinamide	CH ₃ Chiral Chiral Chiral Chiral

Table 1

Entry	Name	Structure
152	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-argininamide	CH ₃ H ₂ N NH Chiral NH NH Chiral NH CF ₃
153	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N~2~-methyl- N~6~-{[(phenylmethyl)oxy]carbonyl}-N-[3- (trifluoromethyl)phenyl]-L-lysinamide	Chiral H ₃ C. H ₂ N CH ₃ O F F F
154	Nalpha-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-tyrosinamide	H ₃ C O CN H Chiral H ₂ N N N CF ₃
155	N~5~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	H ₃ C S N HN O NH ₂

Table 1

Entry	Name	Structure
156	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N~6~,N~6~- dimethyl-N-[3-(trifluoromethyl)phenyl]-L- lysinamide	CH ₃ H ₃ C.N.CH ₃ Chiral
157	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3-[(4- methylpiperazin-1-yl)carbonyl]-5- (trifluoromethyl)phenyl]-L-alaninamide	CH ₃ Chiral N CH ₃ H CH ₃ H CF ₃ N O N O H ₃ C N O
158	3-({N-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-L-alanyl}amino)- N-(3-pyrrolidin-1-ylpropyl)-5- (trifluoromethyl)benzamide	CH ₃ Chiral N CH ₃ H CH ₃ H CF ₃ HN O

Table 1

Entry	Name	Structure
159	3-({N-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-L-alanyl}amino)- N-(2-morpholin-4-ylethyl)-5- (trifluoromethyl)benzamide	CH ₃ Chiral N CH ₃ H CF ₃ HN O
160	3-({N-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-L-alanyl}amino)- N-[2-(dimethylamino)ethyl]-5- (trifluoromethyl)benzamide	CH ₃ Chiral N CH ₃ H CF ₃ H O H O H 3 CF 3
161	3-({N-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-L-alanyl}amino)- N-[3-(4-methylpiperazin-1-yl)propyl]-5- (trifluoromethyl)benzamide	CH ₃ Chiral N CH ₃ H CF ₃ HN O H ₃ C N N N N N N N N N N N N N N N N N N N

Table 1

Entry	Name	Structure
162	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N~2~-methyl- N~6~-{[(phenylmethyl)oxy]carbonyl}-N-[3- (trifluoromethyl)phenyl]-L-lysinamide	CH ₃ HN F F F F CH ₃ O
163	1,1-dimethylethyl ((4S)-4-{[2-amino-5- cyano-6-(ethyloxy)pyrimidin-4-yl]amino}- 5-oxo-5-{[3- (trifluoromethyl)phenyl]amino}pentyl)carb amate	H ₃ C CH ₃ Chiral CH ₃ O NH H ₂ N N H F F
164	(2S)-2-{[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]amino}-3-oxo-3- {[3-(trifluoromethyl)phenyl]amino}propyl acetate	CH ₃ Chiral Chiral Chiral Chiral
165	phenylmethyl N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alpha- glutaminate	CH ₃ O O O CN H N CF ₃

Table 1

Entry	Name	Structure
166	N~2~,N~5~-diacetyl-N~2~-[2- (acetylamino)-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	H ₃ C H CF ₃ Chiral
167	2-(methyloxy)ethyl ((4S)-4-{[2-amino-5- cyano-6-(methylthio)pyrimidin-4- yl]amino}-5-oxo-5-{[3- (trifluoromethyl)phenyl]amino}pentyl)carb amate	O O O O CH ₃ Chiral NH H ₂ N N N CF ₃
168	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-5-morpholin-4-yl- N-[3-(trifluoromethyl)phenyl]-L- norvalinamide	CH ₃ N H ₂ N N H F F F
169	N-((4S)-4-{[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]amino}-5-oxo-5- {[3-(trifluoromethyl)phenyl]amino}pentyl)- N,N-dimethylmethanaminium	CH ₃ CH ₃ Chiral N. CH ₃ H ₂ N N N F F
170	Methyl N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alpha- glutaminate	CH ₃ Chiral OH ₃ C·O H ₂ N N N CF ₃

Table 1

Entry	Name	Structure
171	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N~6~,N~6~- dimethyl-N-[3-(trifluoromethyl)phenyl]-L- lysinamide	H ₃ C. _N .CH ₃ Chiral S.CH ₃ N H ₂ N N H F F
172	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N~2~-methyl-N- {3-[(trifluoromethyl)oxy]phenyl}-L- alaninamide	CH ₃ Chiral N CH ₃ N CH ₃ N CH ₃ N CH ₃ N F F
173	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alpha-glutamine	CH ₃ HO O CN H N CF ₃
174	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-(3- bromophenyl)-N~2~-methyl-L- alaninamide	CH ₃ Chiral Chiral Chiral Chiral
175	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N~1~-[3- (trifluoromethyl)phenyl]-L-glutamamide	CH ₃ Chiral Chiral Chiral Chiral

Table 1

Entry	Name	Structure
176	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-3- (dimethylamino)-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	CH ₃ Chiral Chiral Chiral Chiral
177	'2-(2-amino-5-cyano-6-ethoxy-pyrimidin- 4-ylamino)-4-hydrazinocarbonyl-N-(3- trifluoromethyl-phenyl)-butyramide	CH ₃ NH ₂ Chiral Chiral NH ₂ N N N N N N N N N N N N N N N N N N N
178	N~2~-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-3- (dimethylamino)-N-[3- (trifluoromethyl)phenyl]-L-alaninamide	H ₃ C. O Chiral Chiral H ₂ N N CH ₃ F F F
179	N~2~-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-N-[3-{[2- (dimethylamino)ethyl]oxy}-5- (trifluoromethyl)phenyl]-L-alaninamide	H ₂ N N H F F F O N CH ₃ CH ₃ CH ₃ CH ₃ CH ₃
180	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3-{[2- (dimethylamino)ethyl]oxy}-5- (trifluoromethyl)phenyl]-L-alaninamide	Chiral Chiral Chiral Chiral Chiral Chiral

Table 1

Entry	Name	Structure
181	N~2~-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-N-(3- bromophenyl)-N~2~-methyl-L- alaninamide	H ₃ C·OCNCH ₃ H H ₂ N N N Br CH ₃ O
182	phenylmethyl N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-alpha- glutaminate	H ₃ C.S O O H CF ₃
183	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-O- (phenylmethyl)-N-[3- (trifluoromethyl)phenyl]-L-serinamide	H ₃ C.S CN O H ₂ N N N CF ₃
184	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N~5~,N~5~- bis[2-(methyloxy)ethyl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	S.CH ₃ NO.CH ₃ H ₂ N N CF ₃
185	1,1-dimethylethyl ((4S)-4-{[2-amino-5- cyano-6-(methyloxy)pyrimidin-4- yl]amino}-5-oxo-5-{[3- (trifluoromethyl)phenyl]amino}pentyl)carb amate	H ₂ N N N CF ₃

Table 1

Entry	Name	Structure
186	N~5~-acetyl-N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	CH ₃ O CH ₃ Chiral NH NH CF ₃
187	N~5~-acetyl-N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	O CH ₃ Chiral NH NH CF ₃
188	N~2~-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-N~2~-methyl- N-{3-[(trifluoromethyl)oxy]phenyl}-L- alaninamide	H ₂ N N CH ₃ H OCF ₃
189	methyl 3-({N-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-L- alanyl}amino)-5-(trifluoromethyl)benzoate	H ₂ N N H CF ₃ H CF ₃ CF ₃
190	3-({N-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-L- alanyl}amino)-N-[2-(dimethylamino)ethyl]- 5-(trifluoromethyl)benzamide	Chiral CH ₃ H CH ₃ H CF ₃ N CH ₃ H CH ₃ H CH ₃ H CF ₃ N CH ₃ H CH CH CH CH CH CH CH CH CH

Table 1

Entry	Name	Structure
191	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-3-morpholin-4- yl-N-[3-(trifluoromethyl)phenyl]-L- alaninamide	H ₃ C.S Chiral
192	N~2~-[2-amino-5-cyano-6- (methyloxy)pyrimidin-4-yl]-3-morpholin-4- yl-N-[3-(trifluoromethyl)phenyl]-L- alaninamide	H ₃ C. O Chiral
193	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-3-morpholin-4-yl- N-[3-(trifluoromethyl)phenyl]-L- alaninamide	CH ₃ Chiral H ₂ N N N F F
194	N~5~-(aminocarbonyl)-N~2~-[2-amino-5- cyano-6-(ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	ONH ₂ Chiral OH NH NH H ₂ N NH F F F
195	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-D-lysinamide	SMe N H F F F F F F F F F F F F F F F F F F

Table 1

Entry	Name	Structure
196	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-N-[3- (trifluoromethyl)phenyl]-D-lysinamide	OEt NH ₂ Chiral
197	N~2~-[2-amino-5-cyano-6- (ethyloxy)pyrimidin-4-yl]-O-methyl-N-[3- (trifluoromethyl)phenyl]-L-serinamide	CH ₃ CH ₃ CH ₃ CH ₃ CF ₃ H ₂ N N N CF ₃
198	N~2~-[2-amino-5-cyano-6- (methylthio)pyrimidin-4-yl]-N~5~- (methylsulfonyl)-N-[3- (trifluoromethyl)phenyl]-L-ornithinamide	CH ₃ Chiral O=\$=0 NH H ₂ N N H CF ₃

[0056] <u>Embodiment [0056]:</u> Another aspect of the invention is a pharmaceutical composition comprising the compound according to any one of <u>Embodiments paragraphs [0022]-[0055]</u> and a pharmaceutically acceptable carrier.

[0057] Embodiment [0057]: Another aspect of the invention is a metabolite of the compound or the pharmaceutical composition according to any one of Embodiments paragraphs [0022]-[0056].

[0058] Embodiment [0058]: Another aspect of the invention is a method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of a composition comprising at least one of: the compound according to any of Embodiments paragraphs [0022]-[0055], the pharmaceutical composition according to Embodiment paragraph

[0056], a compound explicitly provided against in Embodiment paragraph-[0022] or [0042], and a pharmaceutical composition comprising a compound, the composition of which was, explicitly provided against in Embodiment paragraph-[0022] or [0042] and a pharmaceutically acceptable carrier.

[0059] Embodiment [0059]: Another aspect of the invention is the method according to Embodiment paragraph [0058], wherein the kinase is p70S6K.

[0060] Embodiment [0060]: Another aspect of the invention is the method according to Embodiment paragraph [0059], wherein modulating the *in vivo* activity of p70S6K comprises inhibition of p70S6K.

<u>Embodiment [0061]:</u> Another aspect of the invention is a method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of a composition comprising at least one of: the compound according to any of <u>Embodiments paragraphs</u> [0022]-[0055], the pharmaceutical composition according to <u>Embodiment paragraph</u> [0056], a compound, the composition of which was, explicitly provided against in <u>Embodiment paragraph</u> [0022] or [0042], and a pharmaceutical composition comprising a compound, the composition of which was, explicitly provided against in <u>Embodiment paragraph</u> [0022] or [0042] and a pharmaceutically acceptable carrier.

[0062] Embodiment [0062]: Another aspect of the invention is a method of screening for modulator of a p70S6K kinase, the method comprising combining either a compound according to any one of Embodiments paragraphs—[0022]-[0055] or a compound, the composition of which was, explicitly provided against in Embodiment paragraph—[0022] or [0042], and at least one candidate agent and determining the effect of the candidate agent on the activity of said kinase.

[0063] Embodiment [0063]: Another aspect of the invention is a method of inhibiting proliferative activity in a cell, the method comprising administering an effective amount of: the compound according to any of Embodiments paragraphs—[0022]-[0055], the pharmaceutical composition according to Embodiment paragraph—[0056], a compound, the composition of which was, explicitly provided against in Embodiment paragraph—[0022] or [0042], and a pharmaceutical composition comprising a compound, the composition of which was, explicitly

provided against in Embodiment paragraph-[0022] or [0042] and a pharmaceutically acceptable carrier.

<u>Embodiment [0064]</u>: Another aspect of the invention is a method of inhibiting abnormal metabolic activity in a cell, the method comprising administering an effective amount of: the compound according to any of <u>Embodiments paragraphs</u> [0022]-[0055], the pharmaceutical composition according to <u>Embodiment paragraph</u> [0056], a compound, the composition of which was, explicitly provided against in <u>Embodiment paragraph</u> [0022] or [0042], and a pharmaceutical composition comprising a compound, the composition of which was, explicitly provided against in <u>Embodiment paragraph</u> [0022] or [0042] and a pharmaceutically acceptable carrier.